

=> d his

(FILE 'HOME' ENTERED AT 13:02:24 ON 18 JAN 2008)  
FILE 'CA' ENTERED AT 13:02:31 ON 18 JAN 2008  
E GOODWIN P/AU  
L1 110 S E3,E8,E30,E34-35  
L2 7 S L1 AND SEQUENCING/TI  
L3 16511 S (RNA OR DNA) (1A) SEQUENCING  
L4 29 S L3 AND RAMAN  
L5 23 S L2,L4 AND PY<2004  
L6 15 S L2,L4 AND PY<2006 AND PATENT/DT  
FILE 'BIOSIS' ENTERED AT 13:08:51 ON 18 JAN 2008  
L7 5 S L5  
FILE 'MEDLINE' ENTERED AT 13:09:07 ON 18 JAN 2008  
L8 3 S L5  
FILE 'CA' ENTERED AT 13:10:56 ON 18 JAN 2008  
L9 413 S L3 AND(PARTICLE OR MICROPARTICLE OR NANOPARTICLE OR BEAD OR  
MICROBEAD OR NANOBEAD OR MICROBALL OR MICROSPHERE OR NANOBALL OR  
NANOSPHERE OR PARTICULATE OR MICROPARTICULATE OR NANOPARTICULATE)  
L10 91 S L9 AND FLUORESC?  
L11 70 S L10 AND PY<2004  
L12 45129 S (COLLECT? OR EXTRACT? OR FILTER? OR CATCH? OR SNARE OR FUNNEL OR  
RESTRAIN? OR HOLD OR POCKET) (6A) (PARTICLE OR MICROPARTICLE OR  
NANOPARTICLE OR BEAD OR MICROBEAD OR NANOBEAD OR MICROBALL OR  
MICROSPHERE OR NANOBALL OR NANOSPHERE OR PARTICULATE OR  
MICROPARTICULATE OR NANOPARTICULATE)  
L13 29043 S (CAPTUR? OR TRAP? OR CONFIN? OR SHEATH OR IMMOBILI?) (6A) (PARTICLE  
OR MICROPARTICLE OR NANOPARTICLE OR BEAD OR MICROBEAD OR NANOBEAD  
OR MICROBALL OR MICROSPHERE OR NANOBALL OR NANOSPHERE OR  
PARTICULATE OR MICROPARTICULATE OR NANOPARTICULATE)  
L14 21 S L11 AND L12-13  
FILE 'BIOSIS' ENTERED AT 13:16:26 ON 18 JAN 2008  
L15 5 S L14  
FILE 'MEDLINE' ENTERED AT 13:17:06 ON 18 JAN 2008  
L16 3 S L14  
FILE 'CA, BIOSIS, MEDLINE' ENTERED AT 13:18:08 ON 18 JAN 2008  
L17 54 DUP REM L5 L6 L14 L7 L15 L8 L16 (21 DUPLICATES REMOVED)

=> d bib,ab 117 1-54

L17 ANSWER 12 OF 54 CA COPYRIGHT 2008 ACS on STN  
AN 139:65712 CA  
TI Confocal **fluorescence** microscopy for single molecule **DNA sequencing**  
IN Nanba, Akihiro; Niimura, Toshinobu; Sawada, Ryuji; Takahashi, Isao  
PA Olympus Optical Co., Ltd., Japan  
SO Jpn. Kokai Tokkyo Koho, 23 pp.  
PI **JP 2003189852** **A** **20030708** **JP 2001-395308** **20011226**  
PRAI JP 2001-395308 20011226  
AB A method and app. are described that demonstrates a new technique for  
rapid and high-throughput single mol. **DNA sequencing**. This sequencing  
technique is based on the successive enzymic degrdn. of **fluorescently**  
labeled single nucleic acid mols., and the detection and identification  
of the released mononucleotides according to their sequential order in a  
microstructured channel. The detection technique is evolved from

confocal **fluorescence** microscopy, with two different laser sources to excite the individual mononucleotides that are labeled with **fluorescent** material. The handling of DNA which is **immobilized** on carrier **beads**, and the detection of the cleaved monomers is performed in optically transparent and biochem. inert microstructures (glass or PMMA) with detection channels of 7  $\mu\text{m}$   $\times$  10  $\mu\text{m}$ . The app. also comprises an optical detector.

L17 ANSWER 14 OF 54 CA COPYRIGHT 2008 ACS on STN  
AN 139:156658 CA

TI Single molecule **Raman** spectroscopy using silver and gold nanoparticles  
AU Kneipp, Katrin; Kneipp, Harald; Dasari, Ramachandra R.; Feld, Michael S.  
CS Massachusetts Institute of Technology, Cambridge, MA, 02139, USA  
SO Indian Journal of Physics, B (2003), 77B(1), 39-47  
AB The authors discuss single mol. **Raman** spectroscopy based on the strongly enhanced **Raman** scattering signals which occur when a target mol. is attached to Ag and Au colloidal nanoparticles. This phenomena known as surface-enhanced **Raman** scattering (SERS) exploits extremely large SERS enhancement factors of about fourteen orders of magnitude, with effective **Raman** cross sections reaching the level of fluorescence cross sections thus enabling a single mol. detection using surface-enhanced **Raman** spectrum. The advantage of this method is that it not only detects a single mol., it also simultaneously provides its structural fingerprint. Also, SERS can be studied under electronic nonresonant conditions, which avoids photobleaching. Detecting single mols. as well as identifying their chem. structures represents the ultimate limit in chem. anal. and is of great practical interest in many fields. This paper gives a brief introduction to single mol. SERS spectroscopy, describes nonresonant single mol. **Raman** expts. at near IR excitation and discuss prospects and limitations of the method.

L17 ANSWER 15 OF 54 CA COPYRIGHT 2008 ACS on STN  
AN 139:47668 CA

TI Progress towards single-molecule DNA **sequencing**: a one color demonstration  
AU Werner, James H.; Cai, Hong; Jett, James H.; Reha-Krantz, Linda; Keller, Richard A.; **Goodwin, Peter M.**  
CS Bioscience Division, Los Alamos National Laboratory, Los Alamos, NM, 87545, USA  
SO Journal of Biotechnology (2003), 102(1), 1-14  
AB Single mols. of fluorescently labeled nucleotides were detected during the cleavage of individual DNA fragments by a processive exonuclease. In these expts., multiple (10-100) strands of DNA with tetra-Me rhodamine labeled dUMP (TMR-dUMP) incorporated into the sequence were anchored in flow upstream of the detection region of an ultra sensitive flow cytometer. A dil. soln. of Exonuclease I passed over the microspheres. When an exonuclease attached to a strand, processive digestion of that strand began. The liberated, labeled bases flowed through the detection region and were detected at high efficiency at the single-mol. level by laser-induced fluorescence. The digestion of a single strand of DNA by a single exonuclease was discernable in these expts. This result demonstrates the feasibility of single-mol. DNA

sequencing. In addn., these expts. point to a new and practical means of arriving at a consensus sequence by individually reading out identical sequences on multiple fragments.

L17 ANSWER 22 OF 54 CA COPYRIGHT 2008 ACS on STN  
AN 139:303960 CA  
TI Single-Molecule Imaging and Spectroscopy Using Fluorescence and Surface-Enhanced **Raman** Scattering  
AU Ishikawa, M.; Maruyama, Y.; Ye, J.-Y.; Futamata, M.  
CS Joint Research Center for Atom Technology (JRCAT), Tsukuba, Ibaraki, 305-0046, Japan  
SO Journal of Biological Physics (2002), 28(4), 573-585  
AB We extended single mol. fluorescence imaging and time-resolved fluorometry from the green to the violet-excitation regime to find feasibility of detecting and identifying fluorescent analogs of nucleic-acid bases at the single-mol. level. Using violet excitation, we obsd. fluorescent spots from single complexes composed of a nucleotide analog and the Klenow fragment of DNA polymerase I. Also, we implemented **Raman** imaging and spectroscopy of adenine mols. adsorbed on Ag colloidal nanoparticles to find feasibility of identifying nucleic-acid bases at the single-mol. level. Surface enhanced **Raman** scattering (SERS) of adenine mols. showed an intermittent on-and-off behavior called blinking. The observation of blinking provides substantial evidence for detecting single adenine mols.

L17 ANSWER 30 OF 54 CA COPYRIGHT 2008 ACS on STN  
AN 131:193486 CA  
TI Single molecule detection with surface-enhanced **Raman** scattering and applications in DNA or **RNA sequencing**  
IN Kneipp, Katrin; Kneipp, Harald; Itzkan, Irving; Dasari, Ramachandra R.; Feld, Michael S.  
PA Massachusetts Institute of Technology, USA  
SO PCT Int. Appl., 57 pp.  
PI WO 9944045 A1 19990902 WO 1999-US4167 19990226  
US 2002150938 A1 20021017 US 2002-54729 20020122  
PRAI US 1998-76310P P 19980227  
US 1998-63741 A 19980421  
US 2002-54729 B1 20020122  
AB Surface-enhanced spectroscopy, such as surface-enhanced **Raman** spectroscopy employs aggregates that are of a size that allows easy handling. The aggregates are generally at least ~500 nm in dimension. The aggregates can be made of metal particles of size <100 nm, allowing enhanced spectroscopic techniques that operate at high sensitivity. This allows the use of larger, easily-handleable aggregates. Signals are detd. that are caused by single analytes adsorbed to single aggregates, or single analytes adsorbed on a surface. The single analytes can be DNA or RNA fragments comprising at least one base.

L17 ANSWER 37 OF 54 CA COPYRIGHT 2008 ACS on STN  
AN 129:133269 CA  
TI Detection and identification of a single DNA base molecule using surface-enhanced **Raman** scattering (SERS)  
AU Kneipp, Katrin; Kneipp, Harald; Kartha, V. Bhaskaran; Manoharan,

- Ramasamy; Deinum, Geurt; Itzkan, Irving; Dasari, Ramachandra R.; Feld, Michael S.
- CS G. R. Harrison Spectroscopy Laboratory, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA
- SO Physical Review E: Statistical Physics, Plasmas, Fluids, and Related Interdisciplinary Topics (1998), 57(6), R6281-R6284
- AB Nonresonant **Raman** cross sections of  $\sim 10$ - $16$  cm<sup>2</sup> per mol. are shown to be related to surface-enhanced **Raman** scattering (SERS) on colloidal silver clusters at near-IR (NIR) excitation. The enhancement is independent of cluster sizes between 100 nm and 20  $\mu$ m. These exptl. findings demonstrate that NIR SERS on colloidal silver clusters is an excellent technique for single mol. detection that is applicable for a broad range of mols. including "colorless" biomols., for example nucleotides in **DNA sequencing**. As an example, a single adenine mol. without any labeling is detected based on its intrinsic surface-enhanced **Raman** scattering.
- L17 ANSWER 40 OF 54 CA COPYRIGHT 2008 ACS on STN
- AN 127:356635 CA
- TI Techniques for single molecule sequencing
- AU Dorre, Klaus; Brakmann, Susanne; Brinkmeier, Michael; Han, Kyung-Tae; Riebeseel, Katja; Schwille, Petra; Stephan, Jens; Wetzel, Timm; Lapczynska, Markus; Stuke, Michael; Bader, Raoul; Hinz, Michael; Seliger, Hartmut; Holm, Johan; Eigen, Manfred; Rigler, Rudolf
- CS Abteilung Biochemische Kinetik, Max-Planck-Institut für Biophysikalische Chemie, Göttingen, D-37077, Germany
- SO Bioimaging (1997), 5(3), 139-152
- AB A method is described that demonstrates a new technique for rapid and high-throughput single mol. sequencing. This sequencing technique is based on the successive enzymic degradn. of **fluorescently** labeled single DNA mols., and the detection and identification of the released monomer mols. according to their sequential order in a microstructured channel. The detection technique is evolved from confocal **fluorescence** microscopy, with two different laser sources to excite the individual mononucleotides that are either labeled with tetramethylrhodamine (TMR) or Cyanine5 (Cy5). The handling of DNA which is **immobilized** on carrier **beads**, and the detection of the cleaved monomers is performed in optically transparent and biochem. inert microstructures (glass or PMMA) with detection channels of 7  $\mu$ m  $\times$  10  $\mu$ m. The projected rate of sequencing is  $\approx 100$  bases min<sup>-1</sup>, dependent solely on the rate of the enzymic DNA cleavage.
- L17 ANSWER 45 OF 54 CA COPYRIGHT 2008 ACS on STN
- AN 123:134132 CA
- TI Flow-based continuous DNA **sequencing** via single molecule detection of enzymically cleaved fluorescent nucleotides
- AU Schecker, Jay A.; Goodwin, Peter M.; Affleck, Rhett L.; Wu, Ming; Martin, John C.; Jett, James H.; Keller, Richard A.; Harding, John D.
- CS Los Alamos National Laboratory, Center Human Genome Studies, Los Alamos, NM, 87545, USA
- SO Proceedings of SPIE-The International Society for Optical Engineering (1995), 2386, 4-12

AB The development of the rapid, continuous DNA sequencing technol., based on single mol. detection of fluorescently-tagged nucleotides, has proceeded along sep. research fronts, each with specific goals: the faithful replication of long sequences of template DNA using one or more fluorescent nucleotide analogs, the incorporation and stable mounting of a single DNA strand into a flow, chamber, the enzymic cleavage of labeled DNA by exonucleases, and the detection of single fluorescent nucleotides in a flow stream by the method of time-gated photon counting. Each individual goal of the sequencing technol. has now been realized, and the authors have begun integrating these efforts to demonstrate the feasibility of flow-based sequencing. The authors are currently detecting photon bursts from TRITC-labeled nucleotides which have been cleaved from DNA suspended in the flow cell. The sample size is estd. to be tens of DNA strands.

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STN INTERNATIONAL LOGOFF AT 13:18:53 ON 18 JAN 2008